

The Aid which Experimentation on Animals has given to the Science and Practice of Medicine,

BY

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The great majority of those who desire the total abolition of experiments on animals are actuated by the most praiseworthy motives, for they feel sympathy with suffering and desire to prevent it. Either consciously or unconsciously they adopt as their motto the words of Coleridge in his *Ancient Mariner*:

"He prayeth well who loveth well
"Both man and bird and beast;
"He prayeth best who loveth best
"All things both great and small;
"For the dear God who loveth us
"Hath made and loveth all."

But most of these people are ignorant of the fact, and a few unfortunately wilfully ignore it, that if they succeed in their agitation they are reversing the order of things in the poet's lines. They are putting the beast before man, and if they stop experiments on animals they will increase, out of all proportion, pain and suffering in man.

Struggle for Existence.

Experimentation is the condition under which all living beings exist. Each alteration in structure or function is an experiment made by nature upon them, and when the experiment is successful, so that the animals become adapted to their environment, they survive in the struggle for existence; where it is unsuccessful they die out.

Epidemic Diseases.

Experiments are sometimes made on an enormous scale by epidemic diseases, which sweep away thousands of people, leaving as the survivors those who have most powers of resistance, a power which they may transmit to their descendants; so that a disease which, like measles, is comparatively harmless in a population where it is endemic, as in this country, may become a devastating pestilence when introduced into a country like the Fiji Islands, where it was formerly unknown.

Sufferings of Mankind.

But it is not by means of epidemic diseases only that nature experiments on mankind. Cancerous tumours in various parts of the body may give rise to the most excruciating agony, disease of the stomach or intestines may cause such distress that the sufferer desires death rather than life, disease of the heart may reduce the most powerful athlete to the condition of a bedridden invalid, and hæmorrhage and consequent softening of the brain may bring the intellect of the keenest man of business, of the most polished writer, of the deepest thinker, or of the most sagacious and far-seeing statesman, below that of a pig in a sty.

Position of Medical Men.

It is because medical men are brought daily face to face with these awful results of disease that they are anxious that no unnecessary difficulties should be placed in the way of

those who are trying, by experiments on animals, to learn how to prevent or cure them. Medical men also know only too well that each effort they make to alleviate pain or cure disease is an experiment made on their patient. In the ordinary phrase, they "try the remedy"; but it does not always succeed, and in those cases where they use remedies with the greatest certainty of success, it is because the nature of the disease and the action of their remedies have already been accurately ascertained by experiments on animals.

Alleged Inutility of Vivisection.

The objection is sometimes raised to experimentation on animals that such experimentation is unnecessary, and that observation at the bedside ought to be amply sufficient to discover the causes and treatment of disease.

Refutation of this Objection.

Theoretically, this might be so, but practically it is not, for the problems of life, disease and death, as presented to us by observation on man, are too complicated, and it is only by simplifying them and learning by experimentation on animals the various factors of which they are composed, that we can solve them at all.

Circulation of the Blood.

The circulation of the blood may be said to be the foundation stone of all medical knowledge. For thousands and thousands of years blood vessels had been cut in battle and blood had run in streams, yet the fact that it circulated in the body from the heart to the limbs and back to the heart again, and did not simply oscillate backwards and forwards, remained unknown until Harvey discovered the circulation by systematic experiments on animals.

Knowledge regarding the Pulse.

Both before and since Harvey, physicians have felt the pulse in patients, but the causes of alterations in its rate, volume and strength were not known until about half-a-century ago, when Humboldt and others showed that heat quickens the beats of the heart and thus explained the rapid pulse in fever, and more recently still the experiments of the Webers, of Ludwig, and of his scholars upon animals showed the effects of the nerves in altering the condition both of the heart and vessels.

Diagnosis of Cardiac Disease.

The sounds of the heart were known to Harvey, but the true significance of alterations in them which now allows of valvular disease to be so readily recognised by every doctor, was only definitely discovered in 1836, by a Committee of the British Association by experiments on animals.

Benefits to Patients in Heart Disease from Regimen.

The benefits which patients suffering from heart disease receive from the use of drugs, great as they are, are much exceeded by the benefits they derive from the rules for the proper regulation of diet and exercise, which a knowledge of their condition allows to be laid down, and which, if followed out, not only prolong the patient's life, but prevent for a long time, it may be for years, the occurrence of any distressing symptoms. All these benefits they owe to experiments on animals.

Benefits from Remedies.

When such symptoms do appear they can often be relieved, and life prolonged, by the use of drugs, but the exact knowledge of the action of these remedies which enables us to use them with success is almost entirely derived from experiments on animals. Even when I was a student digitalis,

which is one of the commonest and best of these remedies, was generally regarded as a depressant of the heart, to be avoided in cases where the heart was weak, whereas we now know from experiments upon animals that the reverse is the case, and that it is a powerful cardiac tonic and restores strength to a failing heart. Many other remedies having a somewhat similar action, and in certain cases preferable to digitalis itself, have been introduced into medicine of late years, in consequence of the nature of their action having been discovered by experiments on animals.

Blood Pressure.

The amount of pressure within the blood vessels is of the utmost importance in reference to medicine, because if it falls too low, the organs, especially the nervous system, are imperfectly nourished and there is a danger of syncope, while, if it is too high, the heart on the one hand may find that the resistance is too great for it to overcome, and the patient may suffer from cardiac failure or from angina pectoris, or, on the other hand, the great pressure may burst a vessel in the brain, and lead to paralysis, senile decay or death. The amount of pressure in the blood vessels was first ascertained by the Rev. Stephen Hales, and published under the auspices of the Royal Society; but the conditions which regulate it and prevent it from rising too high or falling too low, have been chiefly worked out by Ludwig and his pupils.

Angina Pectoris.

By finding in a case of angina pectoris that the blood pressure rose too high, and having learned through experiments on animals that nitrite of amyl would lower the pressure, I applied the drug to the treatment of the disease with perfect success. It might be said that my observation on the rise of

blood pressure in the disease was not due to experiments upon animals because it was made by sphygmographic observations on a patient, but it was by experiments upon animals that Marey learned how to interpret the tracings of the sphygmograph which he had invented.

Prevention of Cardiac Failure and Apoplexy.

Other substances having the power of dilating the vessels have been since discovered by experiments upon animals, and medical men are now beginning to employ them with success in keeping down the blood pressure of their patients, and thus preventing cardiac failure on the one hand, or damage to the brain by bursting of a blood vessel on the other.

Treatment of Dropsy.

Dropsy, which is one of the most common consequences of cardiac disease, has long been treated by various herbs, but it is only through experiments on animals that we have learned what the drugs we are employing are actually doing, and how to prevent their doing harm instead of good. As an example of this I may mention that digitalis, which is one of our best diuretics in cardiac dropsy and in proper doses increases the flow of urine and removes water from the body, in an overdose will stop the action of the kidneys entirely by contracting their blood vessels. This effect may be to a great extent counteracted by administering a drug which will dilate the blood vessels along with digitalis, and if in addition to this we use some substances which stimulate the kidneys directly we get the very best possible results.

Benefits resulting to the treatment of Diseases of the Circulation.

To sum up, we may say that, in all diseases and disorders of the circulation, the knowledge which enables us to detect and to cure them has been obtained directly or indirectly by experiments upon animals.

Respiration.

In regard to respiration the gains of medicine have been fewer than in regard to the circulation; but the most powerful of all respiratory stimulants, and the one which is most generally employed when everything else fails, is strychnine. The use of this is entirely due to experiments upon animals. It is through experiments on animals also that the nature of the most dreadful of all respiratory diseases, namely phthisis, has been discovered, and we have already begun to lessen and we trust, ere long, will stamp out the disease.

Digestion.

Remedies which act upon the digestive tract, and more especially emetics and purgatives, have been used from time immemorial by man, but it is only through experiment upon animals that we have obtained such knowledge of the processes of digestion as enables us to aid digestion by the employment of such digestive ferments as pepsine.

Abdominal Surgery.

Even the skilful surgical treatment of abdominal disease, which is now saving so many lives and curing so many painful conditions which would otherwise be hopeless, owes its origin to experiments upon animals, for it was Blondlot and Bernard who showed that the stomach and pancreas might be operated upon without injury to the animal's life, and Ludwig and Thiry who first performed upon animals resection of the intestine, an operation which is now frequently done by surgeons for the cure of cancer. The technique of their operation as modified by Paschutin was described by me a third of a century ago in Burdon Sanderson's Handbook for the Physiological Laboratory, and although this Handbook has been reviled and called the Handbook of Torture, my own belief is that it served to bring these operations before the notice of those who were actually at the time in practice, or who afterwards became surgeons.

Diabetes.

It is to Bernard's experiments that we owe a knowledge of the power of the liver to form sugar and of the connection of this with diabetes. His researches have had a very practical important bearing upon the treatment of this disease, for it was these researches which indicated the necessity for a diet free from sugar or starch in patients suffering from it.

Internal Secretions.

Still more important, however, were his researches as affording the first indication of what is now known as internal secretion. The liver pours bile out into the intestine, but it pours back into the blood the sugar which it forms.

Other glands have now been found to have also the function of pouring substances which they form into the blood and thereby influencing to an enormous extent the growth and nutrition of the body.

Myxœdema and Cretinism.

One of the most striking examples of the effect of experiment upon animals on the treatment of disease is afforded by the administration of thyroid gland in myxœdema and cretinism. Experiments upon animals have shown that these conditions depend upon absence or atrophy of the gland in patients, and by giving the gland artificially not only can the dull heavy look, the swelled face, the slow movements and chilly feelings of myxœdematous patients be removed and a healthy condition restored, but cretinoid children, stunted in body and dwarfed in mind, may be made to grow up strong and healthy, so that when the treatment is begun in time the apparently impossible feat of adding a cubit to their stature is frequently performed.

Sleeplessness and Pain.

Sleeplessness and pain are two of the greatest miseries that human being can endure, yet not more than half-a-century ago we were practically confined to only one remedy, opium, with which to combat both, for though henbane was sometimes used its results were inconstant and untrustworthy.

Hypodermic Medication.

One of the most important inventions in regard to the relief of pain may be considered to be the introduction of hypodermic medication, and this was the results of experiments made upon animals, first of all by Christopher Wren, afterwards by Magendie and Orfila, and described by the late Sir Robert Christison to Dr. Alexander Wood, who invented the hypodermic syringe.

New Remedies to lessen Pain.

In addition to opium and alkaloids we now have many other substances to lessen pain, cocaine with all its derivatives, eucaine, ocoine, nirvanin, anæsthesin, etc., as well as another set of remedies, antipyrin, phenacetin, phenalgin, aspirin, etc., which can often be used in place of opium or its derivatives with great success in removing pain.

Remedies for Sleeplessness.

We have a whole series also of hypnotics, chloral, sulphonal, trional, veronal, paraldehyde. All those new substances for lessening pain and producing sleep were discovered by means of experiments upon animals.

Knowledge of the conditions of Sleep.

When I was a student, the distress and sleeplessness of fever were combated by a mixture of opium and tartar emetic, but their administration was purely empirical, and no one

knew that in mixing the two we were using the opium to quiet the brain, and the tartar emetic to lessen the circulation. We can now give, in addition to actual nerve sedatives, drugs which will slow the circulation, either directly or by reducing the temperature in fever.

Antipyretics.

In those days we had no antipyretics, and these have been introduced, with few, if any exceptions, through experiments upon animals.

Surgical Treatment of Nerve Centres.

The surgical treatment of tumours of the brain or diseases of the spinal cord is also entirely due to experiments upon animals.

Experimentation for purposes of Teaching.

In other departments of medicine experiments upon animals for the purposes of research have done more to advance science than ages of mere observation.

Many people say that while they are ready to acknowledge this and to allow experiments for research, they do not think that animals should be employed for the purpose of demonstration. I may possibly be regarded as a prejudiced witness, but at least I have the advantage of being able to speak from my own experience regarding lectures without experiments, which I listened to as a student, and learning by actual demonstration upon living animals which I had abroad ; and I can say that the difference between the knowledge gained in these two ways was as great as between the knowledge gained by reading of how to put a bandage on a broken limb and the knowledge gained by actually applying it.

Anæsthesia in Demonstrations.

For my own part, I should object to the infliction of pain upon animals for the purpose of demonstration; but I am perfectly convinced that demonstration upon fully narcotised animals of facts already known, for the purpose of teaching students, is indispensable to their acquiring such knowledge as may enable them to practise their profession to the greatest possible advantage to their patients.

Relaxation of Present Restrictions.

Instead of the laws against the experimentation upon animals being made more stringent, it seems to me that they ought to be very much relaxed.

Harm done by Present Restrictions.

While medical men have been prevented from gaining knowledge patients have been dying in thousands because of our ignorance. As an example of this I may say that in 1878 Sir Joseph Fayrer and I made a number of experiments upon antidotes to snake venom. We showed that several substances had the power of destroying the venom when mixed with it before injection. We did not then succeed in preventing death when the antidote was used after the poison had already been injected. Before we could do this our experiments were cut short by the difficulties occasioned by the Vivisection Act, and it was only through the invention of a means of giving chloroform for very many hours together, that we were able in 1904 to take up the subject again, along with Captain Leonard Rogers. We then found that it was possible to overtake the poison after injection, and thus save the animal's life. Since his return to India, Captain Rogers has had opportunities of testing the effect of the antidote upon people actually bitten by snakes of all sorts, and has now saved twenty cases which would otherwise almost certainly

have died. When the antidote becomes more commonly employed throughout countries infested with snakes, we may reasonably expect that the number saved will be enormously greater. In India alone it is estimated that 20,000 people die yearly from snake bite. How many of these might have been saved by our research on the use of the antidote had it not been interrupted, it is impossible to say.

Prevention of Infective Disease.

As evidence on this subject will be given by others, I have not even touched upon what are really the greatest attainments of medical science, viz.: the discovery of the nature and proper treatment of infective diseases, and the number of lives and the amount of suffering saved by the introduction of antiseptics. It is impossible to over-estimate the value of anti-diphtheritic serum, which has robbed of its terrors the most dreaded scourge of the nursery. These gains are due to experiments upon animals; and it is not only men who participate in the results, for animals also share in them. The ravages of tuberculosis, glanders and anthrax, have been controlled, and these diseases themselves may possibly at no very distant date be stamped out. As I said at the beginning of my evidence, I believe that the agitation against experiments upon animals is due to ignorance. The evidence obtained by this Commission will, I hope, completely remove this ignorance, and thereby put an end to the so-called anti-vivisection agitation.

10.
ON THE USE
OF

NITRITE OF AMYL IN ANGINA PECTORIS.

By T. LAUDER BRUNTON, B.Sc., M.B.,

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Few things are more distressing to a physician than to stand beside a suffering patient who is anxiously looking to him for that relief from pain which he feels himself utterly unable to afford. His sympathy for the sufferer, and the regret he feels for the impotence of his art, engrave the picture indelibly on his mind, and serve as a constant and urgent stimulus in his search after the causes of the pain, and the means by which it may be alleviated.

Perhaps there is no class of cases in which such occurrences as this take place so frequently as in some kinds of cardiac disease, in which angina pectoris forms at once the most prominent and the most painful and distressing symptom. This painful affection is defined by Dr. Walshe as a paroxysmal neurosis, in which the heart is essentially concerned, and the cases included in this definition may be divided into two classes.

In the first and most typical, there is severe pain in the precordial region, often shooting up the neck and down the arms, accompanied by dyspnœa, and a most distressing sense of impending dissolution. The occurrence and departure of the attack are both equally sudden, and its duration is only a few minutes.

In the second class, which, from its greater frequency, is probably the more important, though the pain and dyspnœa may both be very great, the occurrence of the attack is sometimes gradual, and its departure generally so; its duration is from a few minutes to an hour and a half or more, and

the sense of impending dissolution is less marked or altogether absent.

Brandy, ether, chloroform, ammonia, and other stimulants have hitherto been chiefly relied upon for the relief of angina pectoris; but the alleviation which they produce is but slight, and the duration of the attack is but little affected by them.

In now publishing a statement of the results which I have obtained in the treatment of angina pectoris by nitrite of amyl, I have to observe that the cases in which I employed this remarkable substance belonged rather to the second than the first of the classes above described.

Nitrite of amyl was discovered by Balard; and further investigated by Guthrie,* who noticed its property of causing flushing in the face, throbbing of the carotids, and acceleration of the heart's action, and proposed it as a resuscitative in drowning, suffocation, and protracted fainting.

Little attention, however, was paid to it for some years, till it was again taken up by Dr. B. W. Richardson, who found that it caused paralysis of the nerves from the periphery inwards, diminished the contractility of the muscles, and caused dilatation of the capillaries, as seen in the web of the frog's foot.

Dr. Arthur Gamgee, in an unpublished series of experiments, both with the sphygmograph and hæmadynamometer has found that it greatly lessens the arterial tension both in animals and man; and **it was these experiments**—some of which I was fortunate enough to witness—which led me to try it in angina pectoris.

During the past winter there has been in the clinical wards one case in which the anginal pain was very severe, lasting from an hour to an hour and a half, and recurring every night, generally between 2 and 4 a.m.; besides several others in whom the affection, though present, was less frequent and less severe. Digitalis, aconite, and lobelia inflata were given in the intervals, without producing any benefit; and brandy and other diffusible stimulants during the fit produced little or no relief. When chloroform was given, so as to produce partial stupefaction, it relieved the pain for the time; but whenever the senses again became clear, the pain was as bad as before. Small bleedings, of three or four ounces, whether by cupping or venesection, were, however, always beneficial; the pain being completely absent for one night after the

* 'Journal of the Chemical Society,' 1859.

operation, but generally returning on the second. As I believed the relief produced by the bleeding to be due to the diminution it occasioned in the arterial tension, it occurred to me that a substance which possesses the power of lessening it in such an eminent degree as nitrite of amyl would probably produce the same effect, and might be repeated as often as necessary without detriment to the patient's health. On application to my friend Dr. Gamgee, he kindly furnished me with a supply of pure nitrite, which he himself had made; and on proceeding to try it in the wards, with the sanction of the visiting physician, Dr. J. Hughes Bennett, my hopes were completely fulfilled. On pouring from five to ten drops of the nitrite on a cloth, and giving it to the patient to inhale, the physiological action took place in from thirty to sixty seconds; and simultaneously with the flushing of the face the pain completely disappeared, and generally did not return till its wonted time next night. Occasionally it began to return about five minutes after its first disappearance; but on giving a few drops more it again disappeared, and did not return. On a few occasions I have found that, while the pain disappeared from every other part of the chest, it remained persistent at a spot about two inches to the inside of the right nipple, and the action of the remedy had to be kept up for several minutes before this completely subsided. In almost all the other cases in which I have given it, as well as in those in which it has been tried by my friends, the pain has at once completely disappeared. In cases of aneurism, where the pain was constant, inhalation of the nitrite gave no relief, but where it was spasmodic, or subject to occasional exacerbations, it either completely removed or greatly relieved it. It may be as well to note that in those cases in which it failed small bleedings were likewise useless.

From observations during the attack, and from an examination of numerous sphygmographic tracings taken while the patients were free from pain, while it was coming on, at its height, passing off under the influence of amyl, and again completely gone, I find that when the attack comes on gradually the pulse becomes smaller and the arterial tension greater as the pain increases in severity. During the attack the breathing is quick, the pulse small and rapid, and the arterial tension high, owing, I believe, to contraction of the systemic capillaries. As the nitrite is inhaled the pulse becomes slower and fuller, the tension

diminished, and the breathing less hurried. On those occasions when the pain returned after an interval of a few minutes, the pulse, though showing small tension, remained small in volume, and not till the volume as well as tension of the pulse became normal did I feel sure that the pain would not return.

As patients who suffer from angina are apt to become plethoric, and greater relaxation of the vessels is then required before the tension is sufficiently lowered, I think it is advisable to take away a few ounces of blood every four weeks. When the remedy is used for a long time, the dose requires to be increased before the effect is produced. A less quantity is sufficient when it is used with a cone of blotting-paper, as recommended by Dr. Richardson, than when it is poured on a large cloth. From its power of paralysing both nerves and muscles, Dr. Richardson thinks it may prove useful in tetanus; and I believe that, by relaxing the spasm of the bronchial tubes, it might be very beneficial in **spasmodic asthma**. I have tried it in a case of epilepsy, but the duration of the fit seemed little affected by it. It produces relief in some kinds of **headache**, and in one of **neuralgia of the scalp** it relieved the severe shooting pain, though an aching feeling still remained.

While **cholera** was present in Edinburgh during last autumn, Dr. Gangee proposed it as a remedy during the stage of collapse, a condition in which there are good grounds for supposing that the small arteries, both systemic and pulmonic, are in a state of great contraction. No well-marked case afterwards occurring in the town, he was deprived of an opportunity of putting it to the test; but it is a medicine well worthy of a trial, and, should another epidemic unhappily occur, it may prove our most valuable remedy.

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NITRITE OF AMYL IN ANGINA
PECTORIS.

BY

T. LAUDER BRUNTON, M.D.

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Nitrite of Amyl in Angina Pectoris. By T. LAUDER
BRUNTON, M.D. Communicated by J. BURDON
SANDERSON, M.D. *Read February 11th, 1870.*

WILLIAM H—, æt. 26; formerly a blacksmith, now a toll-keeper; admitted to Ward I, Royal Infirmary, Edinburgh, December 7th, 1866.

Antecedent history.—Patient was strong and healthy till his tenth year, when he was confined to bed for six months by a severe attack of rheumatism. During the next twelve years he had four other less severe attacks, and after recovering from the last of these his feet began to swell during the day.

In April, 1866, he had a seventh attack, which lasted for a month, and six weeks after it was over he noticed an unusual palpitation of his heart, for which he entered the infirmary, and remained there three weeks, but left unrelieved. The palpitation gradually increased till he felt it along the line of the carotids as high up as the ears; and in November last he began to feel besides a dull heavy pain about the left nipple. At first this came on every three days, usually during the night, and lasted half an hour. During the day he felt little inconvenience from the palpitation, unless he exerted himself.

On admission the pain was no longer confined to the region of the left nipple, but was worst along the right border of the sternum, and extended up to the right arm. This pain was more severe if he walked about much, otherwise he felt well. Professor MacLagan had charge of the clinical wards at this time, and the patient was treated for six weeks with tincture of aconite, and then with tincture of digitalis; but under these remedies the pulse became intermittent, and the pain was not relieved by either, and rather aggravated by digitalis. They were therefore discontinued, the digitalis being stopped on January 31st. During their employment wet cupping over the cardiac region to the extent of ᠑iv temporarily relieved the pain.

February 1st, Professor MacLagan's term of office having expired, Professor Bennett took charge of the clinical wards.

On February 5th the patient began to complain of pain in the back, neck, head, thighs, and elbow-joints; he had no appetite, was perspiring profusely, and his pulse was 116, full and strong. Next day the pain was most severe in the shoulders, back, hip, and knee-joints.

On the 8th he was examined by Professor Bennett and the clinical class, and the following was found to be the condition of his circulatory system:—Apex beat $2\frac{1}{4}$ inches below and $2\frac{1}{2}$ inches to the outside of the left nipple. On palpation, pulsation is felt over the whole left front and side of thorax, most strongly between the fourth and sixth ribs, and faintly over the supra-clavicular region.

Cardiac dulness commences at the middle line of the sternum and extends laterally outwards for 5 inches.

A loud, double, blowing sound is heard over the whole of the cardiac region, but is loudest at the base. Over the right sterno-clavicular articulation a single blowing is heard. Pulse 104, strong and jerking. The respiratory system was normal, the skin covered with an acid sweat, the tongue furred, no appetite, urine high-coloured and slightly albuminous. The pain in the joints continued along with pain in the neck in the line of the carotids, but the pain in the cardiac region was absent.

On the 11th the pulse fell to 80, and the pain in the joints diminished, but the patient was still troubled by pain in the left ear, and along the line of the carotids, with violent pulsation in them at night.

On the 18th the rheumatic pains in the joints and shoulders had entirely disappeared, but the pain in the cardiac region came on during the night.

On the 19th four ounces of blood were taken from the arm, with immediate relief to the pain and violent pulsation, and the pain over the heart, which usually came on at 3 a.m., was much less on the ensuing night.

25th.—Patient's appetite remains unimpaired by the pain, and he takes all his food, consisting of steak diet, beef tea, potatoes, and bread. Pil. Colocynt. c. Hyoscy. every other night. Ordered Tinct. Lobeliae, 20 drops three times a day.

27th.—The pain continued to come on during the night. $\bar{\text{z}}$ iv of blood were taken from the arm at 10 p.m. An hour after patient went to sleep, had a good night, and the pain did not come on.

March 3rd.—Pain felt at 11 p.m. in breast and ears. A poultice applied over the breast gave some relief.

6th.—Pain severe at 3 a.m., lasting for about one hour. At 9 a.m. $\mathfrak{z}\text{ij}$ of blood were taken from the arm. At 10 a.m. pulse 76, not so forcible as yesterday.

7th.—No pain during the night.

8th.—Pain came on as usual during the night. Tinct. Lobeliæ to be stopped.

9th.— $\mathfrak{z}\text{j}$ of brandy to be taken when the pain comes on.

10th.—The pain came on in the night and was not relieved by the brandy.

12th.—The pain came on as usual at 3 a.m. A few drops of nitrite of amyl were put on a towel and inhaled by the patient. The primary effect noticed was a suffusion of the face, and the patient felt a glow over his face and chest. The pain disappeared almost simultaneously with the occurrence of these phenomena, but returned in three minutes. He then inhaled 5 drops more; the pain again disappeared and did not return.

16th.—The pain has recurred each night and been relieved by the inhalation of 10 drops of nitrite of amyl. Last night it came on about 10.30 p.m., the same in position and character as before. On the patient's taking 10 drops of nitrite of amyl in $\mathfrak{z}\text{ss}$ of brandy, the pain went away, but returned in three minutes; 5 drops were then inhaled from a towel, and the pain disappeared. He went to sleep in an hour and slept till 3 a.m., when he was awakened by a return of the pain. He drank 10 drops in a little brandy, but, no effect following, he inhaled a few drops. The pain disappeared and did not return.

17th.—Pain came on at 1 a.m.; 10 drops were given internally. The pain was relieved, but returned in a few minutes; 10 drops were then inhaled. The pain disappeared and did not return.

Dr. Bennett, thinking the relief of pain by the amyl might be due to anæsthesia, ordered chloroform to be tried during the attack.

18th.—About 2 a.m. the pain came on as usual, and chloroform was inhaled by the patient. He was only partly put under it, and as soon as he again became completely conscious the pain was found to be present as before; 6 drops of nitrite of amyl were then given by inhalation. The pain disappeared and did not return.

25th.—The pain came on at 1.58 a.m., but was not very

bad. While it was present the pulse was 100, respirations 32. After amyl was given, but the pain not quite gone, the pulse was 130, fell with the disappearance of the pain to 100, and twelve minutes after was 80, and respirations 24.

April 6th.—The pain had come on about 2.35 a.m., and the patient was relieved by a whiff of amyl, but the pain began to return at the end of the sternum, right ear, and right shoulder. The chest was auscultated, but no abnormal sounds could be detected to indicate any coincident spasm of the bronchial tubes.

10th.—Patient continues to have the pain every night, and instead of inhaling the nitrite of amyl from a cloth, does so from the bottle. Two or three inhalations usually suffice to relieve the pain. Up to the 8th he used pure nitrite made by Dr. Gamgee, but this being finished, he then began to use some made by Macfarlan & Co., but the smell of it was not so agreeable, and it sometimes occasioned headache, which the pure amyl never did.

14th.—The pain has been coming on several times during the night, is most intense at a spot two inches inside of the right nipple, remains there after it has gone from the rest of the chest, and is only removed by repeated inhalation. Last night it came on three times and was relieved by amyl each time, but five or six inhalations were required. To-day at 11 a.m. $\frac{3}{4}$ iv of blood were taken from the patient's arm, and he was ordered Potass. Iod. gr. viij, three times a day.

17th.—Pain came on during the night and continued uninterruptedly for one hour and a half. By Dr. Bennett's order no amyl was taken, in order to determine whether the relief of the pain was due to it or to some change in the symptoms independent of it. Three dry cups were applied over the cardiac region. They did not relieve the pain.

18th.—No pain during the night. No amyl taken.

19th.—Very little pain, lasting half an hour. Took no amyl.

May 9th.—Has had the spasmodic pain every night. Last night it came on five times, at intervals of about an hour, and was in each case relieved by inhalation.

15th.—Pain has been rather less during the past two nights. Attention was called to-day to purpuric spots upon both legs, which the patient had noticed some days previously. Gums neither swollen nor tender. His diet for some time past has been beef-steak and potatoes, with porridge and

milk for breakfast. The use of iodide of potassium to be suspended.

17th.—Pain came on severely in the chest a little after midnight. It was worst two inches inside of the right nipple.

Tracing 1.—Oh. 22' a.m. Pulse 104 small, resp. 36. There is a thrill to be heard and felt with the second sound at the apex.

22' 40" 13 drops inhaled from a cloth.

Tracing 2.—Oh. 24' 0" The lever of the sphygmograph has risen very much. The pain has gone, except at a point two inches inside of right nipple.

25' 30" 5 drops more given; pulse 112.

Oh. 28' 0" Pain almost gone; patient now inhaled from the bottle; pulse 100.

Tracing 3.—Oh. 34' 0" Pain has been gone for four minutes, but at 37' it began to return inside the right nipple, and a little more was inhaled.

Oh. 40' 0" Pain quite gone; pulse 92; resp. 28.

Tracing 4.—Oh. 47' 0" Pain did not return.

In these tracings, like the others, the patient's position was unchanged, and neither the band nor pressure screw of sphygmograph was touched.

18th.—Pain came three times last night and was very severe. He has had it during the day three times. The purpuric spots on the legs are much paler. To recommence iodide of potassium.

21st.—The purpuric spots have reappeared on both legs. To stop the Pot. Iod. He had pain last night, but none during the day.

24th.—Bled to ʒiv on account of general uneasiness and powerful pulsations of the heart. The bleeding was immediately followed by a sense of relief.

28th.—The pain has only been absent one night since the bleeding, but it has been much less severe than before it. The sphygmograph was fixed to his arm to-night in order to take a normal tracing for comparison with one to be taken during the attack. This had scarcely been done when the pain unexpectedly came on. The tracing, though unfor-

tunately very imperfect, shows the diminished volume and increased tension of the pulse. In 2 the pain was severe, and 3 was taken after inhalation of amyl.

June 1st.—Condition remains the same, spasmodic pain in the cardiac region occurring every night, but not severe, and easily relieved by a few inhalations of nitrite of amyl. Patient wished to resume his former occupation of toll-keeper, and was to-day discharged at his own request. Recommended to have occasional small bleedings.

Remarks.—In this case of Dr. Bennett's, which by his kind permission I now publish, we have a history of numerous attacks of rheumatic fever, followed by cardiac lesion, which was accompanied by palpitation of the heart, throbbing in the carotids extending as high as the ears, and a spasmodic pain in the chest. This pain was sometimes most severe near the left nipple, and sometimes at the right border of the sternum, but extended over the whole cardiac region, and shot up to the right ear and down the right arm. It used to come on suddenly during the night, generally between midnight and 3 a.m., was accompanied by little or no feeling of dyspnœa, and was somewhat relieved by the patient's sitting up. It generally came on every third night at first, but latterly every night, and was worse when the patient had used much exertion during the day. It was not relieved by tincture of aconite, tincture of lobelia inflata, brandy, or dry cupping over the cardiac region. It was made worse rather than better by tincture of digitalis. It was temporarily relieved by chloroform, but whenever the stupefying effect passed off the pain was as bad as before. It was somewhat relieved by warm poultices to the chest, and was generally absent for one night after a small bleeding, either from the arm or by cupping the chest. Under the use of iodide of potassium the attacks became less frequent, but purpuric spots appeared on the limbs, and each attack was at once relieved by the inhalation of nitrite of amyl. During an attack of rheumatic fever it disappeared completely, again returning with the departure of the rheumatic pains.

Angina pectoris is defined by Dr. Walshe as a paroxysmal neurosis, in which the heart is essentially concerned, and he divides it into pseudo and true angina, which differ mainly in the intensity of the symptoms. Friedrich and others

divide it into functional and organic, according as it is accompanied by cardiac lesion or not. From the absence of a sense of impending death, the present case might be reckoned as one of pseudo-angina, but in the intensity of the pain and the manner of its radiation it more closely resembles true angina. As cardiac lesion was present, it belongs to the class organic angina.

Various opinions have been advanced as to the pathology of this disease, some saying it is a mere brachio-thoracic neuralgia, but most holding that it is a neuralgic affection of the cardiac plexus. Some are of opinion that it is associated with cramp of the heart, others with weakness of that organ.

Eichwald * thinks that there is not only weakness of the heart, but a mechanical impediment to its action, produced by irritation of its regulating nerves, and that the pain is caused by unavailing efforts to overcome this obstacle. Nothnagel † states that during angina there is pallor and coldness of the extremities, small pulse, and other symptoms of a cramp-like contraction of the systemic arteries, and that the spasm is relieved by remedies which cause their relaxation, such as warm baths and friction.

It is quite possible that the pathology of all cases classed under angina pectoris is not the same, and that the differences of opinion are not due merely to the want of exact methods of observation. What the nature of the attack was in the present case may be learned to some extent from an examination of the sphygmographic tracings, which were begun by direction of Dr. MacLagan, and continued during the time the case was in the wards under the care of Dr. Bennett. In taking these tracings, the instrument, which was one of Marey's, without any means of estimating the pressure employed, was applied to the arm above the end of the radius, as it was found to cause pain when applied over the bone for any length of time. The amplitude of the curve thus obtained is greater, and it did not occur to me, till after studying the physiology of the circulation under Professor Ludwig, that in such cases as the present, where sudden changes occur in the vessels, I was increasing the fallacy which the variation in the height of the lever from turgescence of the tissues produces, and which may be confounded with a rise from increased tension in the vessels.

* 'Würzburg med. Zeitschr.' iv, 249; 'Cbtl. f. med. Wiss.,' i, 877.

† 'Deut. Arch. f. klin. Med.,' iii, 309; 'Cbtl. med. Wiss.,' v, 715.

Except where marked otherwise, the tracings were all taken with the patient in a recumbent position, and neither the cord by which the instrument was attached to the arm, nor the screw regulating the pressure, was touched during the observation.

The case excited considerable interest, and was carefully observed and commented on by Professor Bennett to the clinical class, and the cardiac lesion was diagnosed by him from the physical signs to be aortic obstruction and regurgitation, with dilatation of the aorta, but no sacculated aneurism.

The tracings confirm this diagnosis, showing in a typical manner the abrupt ascent, terminating in a hook, of each wave, characteristic of the unfilled arteries, which aortic regurgitation produces, and the long and rounded apex of aortic obstruction. There is, however, a marked difference between the tracings from the two radials, the ascent of the wave being more abrupt, the top flatter, and the descent distinctly dichrotic in the right, while in the left the ascent is less abrupt, as shown by the smaller hook at the top; the maximum height is not attained till near the end of the systole, and there is generally little or no dichrotism in the descent. This might be due to aneurism; but there were no physical signs to show its presence, and in the absence of a post-mortem examination, or experiment with a schema, hypotheses as to the cause of difference are of little value.

The tracings taken during an attack were chiefly from the right radial. The only one I got while the pain was actually coming on is unfortunately an imperfect one (No. 1, May 28th). From this tracing, and from those taken when the pain was becoming worse (Nos. 1 and 2 of May 17th), it will be seen that as the pain increased the curve became lower, both the ascent and descent more gradual, and the dichrotism disappeared. This form of curve clearly indicates that the arterial tension is much increased, and this increase can, I think, be due only to contraction of the small systemic vessels, so sudden and so great as well to deserve the name of spasmodic. As I have stated in a former paper,* this increased tension led me to suggest nitrite of amyl to relieve the spasm.† The rapidity with which this increase in tension takes place is shown by the great change which the form of

* 'Lancet,' July 27th, 1867.

† Dr. Bennett, on being informed of the successful result of the first experiment, ordered the inhalation to be continued.

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the pulse has undergone in tracing 1, May 28th, during the short time occupied in re-inking the pen. It would seem from tracings 3 and 4 of the plate that the tension in the right radial was raised more than in the left, and farther experiments with simultaneous tracings are necessary to decide whether the spasm extends to all systemic vessels or to all alike.

At the same time that the tension increases the pulse becomes somewhat quicker, which shows that there is some disturbance of the regulating apparatus of the heart, as normally the increased tension acting on the roots of the vagus should slow the pulse. It has been suggested to me (by Professor Ludwig) that the pain in the heart may be due to irritation of its sensory nerves by the great pressure of the blood, and that in the right arm and neck may be due to the same cause acting on the arterics, those of the right side being possibly contracted more than the left. Whenever the tension was lowered by nitrite of amyl the pain disappeared from the greater part of the cardiac region, the neck, and the arm, but sometimes remained persistent at a point about two inches to the inside of the right nipple. This I think indicates that the tension in the right ventricle was not yet relieved, and the small volume of the pulse (see tracing 3, May 17th) seems to show that the amount of blood passing through the small pulmonary vessels at each systole was small, probably from contraction of their lumen. So long as this condition remained the pain was almost certain to return. It is possible that the right ventricle might not be able to empty itself completely at each systole, was therefore quickly refilled, and consequently contracted frequently, forcing the left ventricle to contract with it, and producing the rapid pulse with small volume seen in tracing 3 of May 17th. The influence of the small vessels of the lungs over the circulation, though in all probability of extreme importance, is a subject of which we know as yet almost nothing.

The question whether the contractile power of either ventricle is lessened during the attack is one which cannot be decided with certainty from the present tracings. Digitalis, which has been recommended on the supposition that the heart is weak during the attack, proved productive in this case of more harm than good, contracting as it does the small vessels.

We may, I think, conclude that the attack in the present

case consisted in a spasmodic contraction of some, if not all, of the small systemic, and probably of the pulmonary vessels, causing great increase in the blood-pressure in both sides of the heart, such as is found in animals after division of the vagi; that this was probably due to a derangement of the vaso-motor system, and accompanied by a derangement of the cardiac regulating apparatus, producing quickened instead of slowed pulsation; that the pain was not originally in the nerves composing the cardiac plexus, but produced by the pressure of the blood on those of the heart and arteries; and, from the alternation of the attacks with rheumatic pains in other parts of the body, that they were of rheumatic origin.